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Breast Cancer and Body Temperature

R. N. LAWSON, M.D., F.R.C.S.[C] and M. S. CHUGHTAI, M.B., B.S.,
Montreal

ABSTRACT

There is frequently a material difference in the metabolic liberation of heat energy between normal and cancer cells. This cannot be accounted for on the basis of an increased circulation. The increased heat in the tumour and surrounding host area as compared to normal tissue can be detected by the aid of modern heat-recording apparatus. New practical temperature-recording techniques, the results of their use and the implications are described.

HUMAN breast cancer is customarily associated with variable increases in the skin temperature overlying the lesion[1] (Fig. 1). The ipsilateral nipple and areolar area are usually involved in the temperature change regardless of the anatomical location of the primary lesion. The temperature rise due to a cancer is variable but averages in the region of 1° C.[2] (Table I). Clinical experience suggests that there is a correlation between the amount of temperature rise and the degree of malignancy. In other words, the hotter the tumour the more rapid and the more virulent its biological

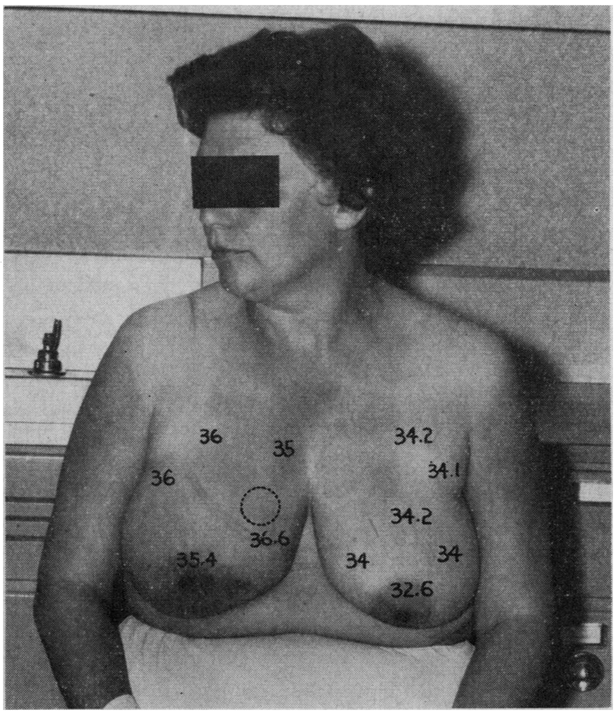

Fig. 1.—Site of breast cancer marked by circle. Skin temperatures are shown in degrees centigrade.

nature. Study of the uptake of β radiation from P^{32} by Hale[3] indicates that the growth of breast carcinoma is not steady and relentless but rather occurs in waves and, in hormone-sensitive cancers, in predictable cycles.

It would seem that the employment of suitable temperature-measuring devices should be of great value not only in early cancer diagnosis but also as a local metabolic yardstick that should help in evaluating the efficiency of treatment of inoperable breast and other cancers. The major clinical effort in cancer therapy lies in the management of advanced lesions.[4] In the past, alleged temperature rises in the neighbourhood of tumours and inflammatory masses have been accounted for by clinicians on the basis of the obvious increased blood and lymphatic vascularity. Our observations indicate that not only is the rationale invalid but the reverse is actually the case. The temperature increases are due to local exothermic conditions.

For instance, the following measurements were made by direct thermister thermometry during mastectomy operations for breast cancer.

Patient	*Tumour temp.*	*Lat. thoracic artery*	*Vein*	*Int. mammary artery*	*Internal mammary vein*
Br........	36.5°C.	34.4°C.	35.0°C.	32.0°C.	33.0°C.
Ho.......	36.7	34.6	35.5	34.1	34.7
Ke.......	36.0	33.5	36.5	(Not done)	
Pe........	36.6	34.0	35.0	31.0	32.0
Au.......	36.8	34.2	36.0	32.0	33.0
Pa.......	36.6	34.4	35.0	32.0	33.0
Fo.......	36.7	34.8	35.2	32.2	32.8

These data indicate that the neoplastic temperatures reflect a state of raised metabolic exchange of the tumour cells similar to that of an inflammatory process. The vascular flow drains off the heat energy and thus actually cools the tumour in spite of serving the tumour's increased metabolic demands. Cooled environmental conditions tend to accentuate temperature differentials, owing to vasomotor reflexes which are more effective away from the lesion.

For the past six years we have been actively concerned and associated with the development of infrared scanning devices capable of mapping and displaying the patterns of radiated heat from the surface of the body. With modern equipment it is possible to display, on an oscilloscope or storage-tube, patterns of heat radiation from the skin in

From the Department of Surgery, Royal Victoria Hospital and McGill University, Montreal.
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TABLE I.

Case No.	Tumour temp. (°C.)	Temp. of identical area opposite breast (°C.)	Temperature difference (°C.)	Room temp. (°C.)	Pathology
221190	37.5	33.0	3.5	21.0	Cancer
212363	36.2	35.0	1.2	21.0	"
213205	36.2	35.0	1.2	21.0	"
213369	36.8	35.8	1.0	21.0	"
214566	36.5	35.0	1.5	21.0	"
215866	36.0	34.25	1.75	21.0	"
216803	36.7	34.2	2.5	21.0	"
216994	37.7	36.0	1.7	21.0	"
217301	36.0	34.0	2.0	21.0	"
217653	36.75	34.5	2.25	21.0	"
218179	36.6	35.5	1.1	21.0	"
220325	37.0	Previous mastectomy		21.0	"
216588	35.8	Previous mastectomy		21.0	"
218368	35.7	34.8	0.9	21.0	"
219954	37.0	35.4	1.6	21.0	"
218344	35.6	35.0	0.6	21.0	"
218716	37.0	36.4	0.6	21.0	"
219007	36.6	36.6	0.0	21.0	"
219646	35.7	35.7	0.0	21.0	"
213202	35.0	35.2	—0.2	21.0	Benign lesion
212280	35.0	35.0	0.0	21.0	" "
212235	34.0	33.7	0.3	21.0	" "
212623	35.0	35.0	0.0	21.0	" "
212563	35.0	35.0	0.0	21.0	" "
212682	33.0	33.0	0.0	21.0	" "
213801	36.0	36.0	0.0	21.0	" "
214707	36.0	35.8	0.2	21.0	" "
214961	36.6	36.0	0.6	21.0	" "
215438	34.0	34.0	0.0	21.0	" "
215189	36.8	36.0	0.8	21.0	" "
215434	36.5	36.5	0.0	21.0	" "
215582	36.2	36.2	0.0	21.0	" "
217084	35.5	35.5	0.0	21.0	" "
217207	35.5	35.7	0.2	21.0	" "
217433	36.5	35.5	1.0	21.0	" "
217822	34.5	33.75	0.75	21.0	" "
218025	35.2	35.2	0.0	21.0	" "
218110	36.25	36.75	0.5	21.0	" "
218330	35.0	35.0	0.0	21.0	" "
218103	35.0	35.0	0.0	21.0	" "
218415	36.2	35.4	0.8	21.0	" "
218533	36.8	36.6	0.2	21.0	" "
218945	34.0	34.0	0.0	21.0	" "
219877	35.2	34.5	0.7	21.0	" "
219750	35.0	35.0	0.0	21.0	" "
219898	36.7	36.7	0.0	21.0	" "
220303	35.5	35.2	0.3	21.0	" "
220610	35.0	35.0	0.0	21.0	" "
220762	36.0	36.0	0.0	21.0	" "
220954	35.0	35.0	0.0	21.0	" "
221046	35.0	35.0	0.0	21.0	" "
221219	35.0	35.0	0.0	21.0	" "
221452	35.0	35.0	0.0	21.0	" "
221554	35.5	35.0	0.5	21.0	" "

Average temperature in cancer: 36.9°C.

Average temperature of benign lesion: 35.4°C.

False negative (temperature increase of less than 1°C. in cancer)—5.

False positive (temperature increase of 1°C. or more in benign lesion)—1.

Fig. 2.—Infrared display of breast showing warmer area over cancer. The heat patterns correspond to the skin temperatures in Fig. 1.

terms of black and white with intermediate shades of grey. The settings on the scanner are adjusted so that the warmer areas appear white and the cooler areas dark in the resultant image[5] (Fig. 2). Infrared applications have lagged behind theoretical information, and the practical problems of applying our knowledge have been incredibly and traditionally frustrating. In spite of discouraging difficulties, many advances are steadily being made. For this we are chiefly indebted to world politics. Government spending designed to improve the efficiency of military applications, many still classified, such as space guidance and detection of oncoming missiles, assures the continuance of intensive research effort in infrared technology. Medical requirements vary considerably from the military. For instance, the radiation wave-lengths that interest us most at body temperature are those in the vicinity of 10 μ. At the moment the most practical military heat-sensing detector cells use cooled indium antimonide elements for fast scanners, because the conductivity of this semi-conductor material responds instantaneously to incoming heat radiation. However, the infrared sensitivity of indium antimonide drops off sharply after 6.5 μ. The problem of cooling these cells has been partly answered by the introduction of thermoelectric frigister units, but extreme cooling for maximum efficiency still remains a cumbersome difficulty. Copper-doped germanium detecting elements that work further out (25-30 μ) in the infrared spectrum have to be cooled to at least minus 230° C. To illustrate this difficulty, it is pointed out that the temperature of liquid nitrogen is only —196° C. Liquid helium is about —269° C., but so far is too expensive for our experimental work.

We have had many technical challenges with our cells because of inadequate vacuum seals and the presence of unwanted absorption bands from moisture. The basic physics of infrared scanners has been previously discussed.[6] It is likely that the accumulation of data supporting biological applications, which is currently taking place, will soon justify the diversion of research funds from military to medical problems.[7] When this occurs, infrared scanning will evolve to play an integral part in every routine physical examination. It will be used primarily for the early detection of vascular and metabolic disorders, since these two groups constitute the bulk of human diseases. The chief advantages of infrared scanning are its ease of application, rapidity and the fact that it is purely passive and may be performed at a distance with minimum inconvenience to the patient.[8] A disadvantage is that only the physiology reflected in the skin can be observed, since radiation of infrared electromagnetic waves is strictly a surface phenomenon. Much remains to be learned about physical factors affecting the emissivity of human skin. The justification of our interest in infrared display is that it gives reliable information which has been heretofore unappreciated and also unattainable by any other means. The advantage of observing a large area at once is obvious, for the surrounding area acts as a control for the point under examination.[9]

Carcinoma cells apparently live and divide at higher than normal body temperatures but do not have the same tolerance to heat increases as normal structures. Crile[10] has demonstrated complete regressions in some experimental animal tumours when subjected to a degree of hyperthermia that is not lethal to host structures. He assumes that the regressions are brought about by immune mechanisms as from antigens liberated from heated tumour cells. His current work on thermal aspects of neoplasia is a distinct step forward in experimental cancer treatment.

The regulation of body temperature gains, losses and distribution is an extremely complex subject. Human life is possible only within the narrow temperature range, and very small fluctuations bring into play an enormous number of adjusting mechanisms. There are wide variations of "normal" temperature values in different parts of the human body and at different periods of the daily cycle. The concept of "core" temperature is now false, misleading and obsolete. The normal range of oral temperatures is from 36.5° C. (97.7° F.) to 37.5° C. (99.5° F.), but this has wide limits of error and does not necessarily represent body temperatures as a whole. For instance, the thyroid gland may have a temperature of 40° C. (104° F.), yet that of the internal mammary artery is usually in the neighbourhood of 32.2° C. (90° F.). It should be apparent that heat energy is produced in various parts of the body from many metabolic sources at widely differing rates. The blood and lymph circulations serve as efficient heat-exchangers, cooling some areas while warming others. The application of local direct temperature transducers, capable of delineating small fluctuations is, then, the obvious way to obtain the most accurate metabolic rate of any given area or organ. It is difficult to understand why this technique has not been already applied to the study of antitumour agents, since specific inhibiting effects should be easily detected.

SUMMARY

Body heat is produced by metabolic exchange at the cellular level; thus an increased metabolic rate is reflected locally by increased heat. Temperature fluctuations can easily be assessed *in situ* by thermisters. Heat radiation from the surface can be visualized by scanners. The influence of agents that affect local metabolic rates can be objectively measured by these new techniques. Temperature recording is certainly the most valuable of any biological measurement, and a thorough knowledge of temperature and its regulation is akin to the Oslerian dictum pertaining to syphilis.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

SURGICAL TREATMENT OF EXOPHTHALMIC GOITRE

A considerable number of publications have recently appeared, emphasizing the importance and frequency of hypertrophy of the thymus in Graves' disease, more especially in cases which die after thyroidectomy. Garre found a persistent thymus in forty-three of fifty-six cases examined post mortem (seventy-seven per cent.). In twenty-four of these cases death was consecutive to thyroidectomy, and in some the hyperplasia of the thymus was associated with hyperplasia of the entire lymphatic system . . . French writers have found persistence of the thymus in fifty per cent. of fatal cases of exophthalmic goitre. Capelle and Bayer found an enlarged thymus in sixty per cent. of cases of Graves' disease, and Melchior believes that it is present in eighty to ninety per cent. of cases of exophthalmic goitre. Rehan is of the opinion that there is a persistent thymus in nearly all the fatal cases of Graves' disease, and most writers on the subject are agreed that its presence considerably increases the gravity of the prognosis, and adds to the risk of operation.

Capelle and Bayer, as a result of very extensive researches, have arrived at the conclusion that a selective heart toxin is formed in the thymus, basing this conclusion on their experimental results . . . Whilst some of the writers on the subject are of the opinion that an enlarged thymus is an absolute contraindication to operation, others are firmly convinced that it is advisable to take the chances of an operation, with the prospect of a cure, rather than to run the risk of allowing the condition to go on. Zesas states that he has found records in literature of twenty-one operations on the thymus for exophthalmic goitre, with sixteen cures, two improvements, and three deaths. It has been found that after removal of the thymus the thyroid gland undergoes marked atrophy.—Herbert A. Bruce: *Canad. Med. Ass. J.*, 3: 2, 1913.